In Utero Treatment of Myelomeningocele with Placental Mesenchymal Stromal Cells - Selection of an Optimal Cell Line in Preparation for Clinical Trials.

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Public Summary:
Background We developed a cell culture assay in order to determine if different lines of placenta mesenchymal stromal cells (PMSCs) can protect cultured neurons from dying when a toxin was administered to the neurons. We then examined if these same PMSC cell lines would have the same neuro protective effect in a fetal lamb model of spina bifida. Methods PMSC lines were created following culture of three different early age human placentas. The lines were labeled as A, B, and C. Their ability to protect dying neurons in a cell culture model was assessed. Spina bifida was created in 28 fetal lambs, and the lambs were repaired with PMSCs seeded on a clinical grade scaffold from each cell line. The number of lambs treated with each different cell line were: 6 with Line A , 7 with Line B, 5 with Line C, and 10 lambs did not receive PMSCs. The lambs motor function post birth was scored with the establish Sheep Locomotor Rating (SLR) scale. A score of 15 denotes normal motor function, while a score of 0 indicates complete hindlimb paralysis. Results Cell culture, Line A and B had a higher neuro protective effect than no PMSCs. Line C did not have a higher neuro protective effect than no PMSCs. Lambs treated with Line A and B had higher motor function scores than lambs that were treated with Line C or with no PMSCs. Conclusion The cell culture model used to assess a PMSC line's ability to protect dying neurons in culture can provide insight on the same cell line's ability to protect neurons in a lamb spina bifida model. Thus, the cell culture model can help predict if a PMSC line will aid in restoring motor function in human spina bifida.

Scientific Abstract:
BACKGROUND: We determined whether in vitro potency assays inform which placental mesenchymal stromal cell (PMSC) lines produce high rates of ambulation following in utero treatment of myelomeningocele in an ovine model. METHODS: PMSC lines were created following explant culture of three early-gestation human placentas. In vitro neuroprotection was assessed with a neuronal apoptosis model. In vivo, myelomeningocele defects were created in 28 fetuses and repaired with PMSCs at 3x10(5) cells/cm(2) of scaffold from Line A (n=6), Line B (n=7) and Line C (n=5) and compared to no PMSCs (n=10). Ambulation was scored as >/=13 on the Sheep Locomotor Rating Scale. RESULTS: In vitro, Line A and B had higher neuroprotective capability than no PMSCs (1.7 and 1.8 respectively vs 1, p=0.02, ANOVA). In vivo, Line A and B had higher large neuron densities than no PMSCs (25.2 and 27.9 respectively vs 4.8, p=0.03, ANOVA). Line C did not have higher neuroprotection or larger neuron density than no PMSCs. In vivo, Line A and B had ambulation rates of 83% and 71%, respectively, compared to 60% with Line C and 20% with no PMSCs. CONCLUSION: The in vitro neuroprotection assay will facilitate selection of optimal PMSC lines for clinical use. LEVEL OF EVIDENCE: n/a. TYPE OF STUDY: Basic science.